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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,854	07/21/2008	Hans Jorgen Blist	056291-5287	8088
9629 7590 10/22/2010 MORGAN LEWIS & BOCKIUS LLP 1111 PENNSYLVANIA AVENUE NW WASHINGTON, DC 20004				
EXAMINER				
NOLAN, JASON MICHAEL				
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1626				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/579,854

**Applicant(s)**

BLIXT ET AL.

**Examiner**

JASON M. NOLAN

**Art Unit**

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 July 2008.  
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-16 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
5) ☒ Claim(s) 9-16 is/are allowed.  
6) ☒ Claim(s) 1 and 4-8 is/are rejected.  
7) ☒ Claim(s) 2 and 3 is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.  
10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☒ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☒ Information Disclosure Statement(s) (PTO/SB/28)  
Paper No(s)/Mail Date 5/17/06, 3/12/08, 4/7/08  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date: \_\_\_\_\_  
5) ☐ Notice of Informal Patent Application  
6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

This Office Action is responsive to Applicant's Preliminary Amendment, filed July 21, 2008. As filed, Claims 1-16 are pending, all of which are currently amended.

#### ***Information Disclosure Statement***

Applicant's information disclosure statements (IDS), filed on May 17, 2006, March 12, 2008, and April 7, 2008 have been considered. Please refer to Applicant's copies of the 1449 submitted herein.

#### ***Priority***

This application is a 371 of PCT/GB04/04964, filed on November 25, 2004. Acknowledgement is made of Applicant's claim for priority to Sweden 0303220-8, filed November 28, 2003; however, said document has not been received by Applicant or the International Bureau. The Examiner respectfully requests that Applicant provide a copy of Sweden 0303220-8.

#### ***Claim Rejections - 35 USC § 102/103***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Obviousness under 35 U.S.C. § 103 is a question of law, but is based on underlying facts of each case. The Supreme Court stated that an invention may be found obvious if it would have been obvious to a person having ordinary skill to try a course of conduct:

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

*KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007).

Although a combination of relevant options in a particular art may be obvious to try, there are instances where an invention would not have been obvious to try:

1) When the inventor would have had to try all possibilities in a field unreduced by direction of the prior art. In other words, when "what would have been 'obvious to try'

would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful" an invention would not have been obvious. *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988). This is another way to express the KSR prong requiring the field of search to be among a "finite number of identified" solutions. 550 U.S. at 421.

2) An invention is not obvious to try where vague prior art does not guide an inventor toward a particular solution. A finding of obviousness would not obtain where "what was 'obvious to try' was to explore a technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." *O'Farrell*, 853 F.2d at 903. This expresses the same idea as the KSR requirement that the identified solutions be "predictable." 550 U.S. at 421.

*In the instant application*, Claims 1 & 4-8 are drawn to a method of resolving an optionally substituted mandelic acid (i.e., a carboxylic acid) via the formation of a salt with a cyclic amide base. The molar ratio of mandelic acid to amide base is 1:0.25-0.75 in any solvent (Claim 1), but preferably ethyl acetate (Claim 5).

Claims 1 & 4-8 are rejected under 35 U.S.C. § 102(b) as anticipated by SAMUEL H. WILEN, TABLES OF RESOLVING AGENTS AND OPTICAL RESOLUTIONS (Edited by Ernest L. Eliel), 1972, pp. 18-23, 49-78, & 121-131 ("Wilen"); or, in the alternative, Claims 1 & 4-8

are rejected under 35 U.S.C. § 103(a) as being unpatentable over Wilén in view of MICHAEL B. SMITH & JERRY MARCH, MARCH'S ADVANCED ORGANIC CHEMISTRY (5<sup>th</sup> edition) 2001, 151-155 & 199-202 ("March"); US 1,867,274; US 4,260,815; US 4,198,524; US 4,239,912; and US 4,259,521.

1. *Determining the scope and contents of the prior art –*

Wilén discloses tables that review the literature of resolutions up the publication in 1972. Disclosed on p. 72, e.g., is mandelic acid, as well as some optionally substituted derivatives thereof. The resolving agents used for the resolution of such compounds include, *inter alia*, brucine. Brucine is a cyclic amide. With respect to anticipation, Wilén does not disclose the molar ratio between mandelic acid and cyclic amide, *infra*, but the preferred ratio is within the knowledge of one of ordinary skill in the art (i.e., since a mole of a racemic mixture contains half a mole of each enantiomer, then only a half a mole, or slight excess of half, is needed to form the preferred salt for fractional crystallization. The secondary references make this clear).

March states: "A pair of enantiomers can be separated in several ways, of which conversion to diastereomers and separation of these by fractional crystallization is the most often used. . . . Most resolution is done on carboxylic acids and often, when a molecule does not contain a carboxyl group, it is converted to a carboxylic acid before resolution is attempted."

US 1,867,274 discloses a process for the resolution of racemic mandelic acid with ephedrine in 95% alcohol. The ratio of mandelic acid to ephedrine is "slightly more than half, desirably about 60%." See p. 2, ll. 94-104. Also disclosed is a process to

obtain further resolved mandelic acid salt by separation and racemization (treatment of the mother liquor with acid) followed by repeating the previous steps (this process is generically referred to as "recycling"). See, e.g., p. 2, lines 122-130 and p. 3, ll. 1-43.

US 4,260,815 discloses a process for the resolution of racemic mandelic acid with 2-amino-1-butanol, and subsequent recycling of the mother liquor. See col. 1.

US 4,198,524 discloses a process for the resolution of racemic mandelic acid with "alanine, methionine,  $\alpha$ -aminobutyric acid or the like (amino acids)." See col. 3. Also disclosed is the process of cooling the solution before filtering, preferred molar ratios, and recycling. See, e.g., col. 3, ll. 53-70 & col. 4, ll. 1-70.

US 4,239,912 discloses a process for the resolution of racemic mandelic acid with "an optically active 2-benzylamino-1-butanol." See col. 2. Also disclosed are process steps such as cooling the solution before filtering, preferred molar ratios, and recycling. See, e.g., cols. 2-4.

US 4,259,521 discloses a process for the resolution of racemic mandelic acid with "an optically active 2-benzylamino-1-butanol." See col. 2. Also disclosed are process steps such as cooling the solution before filtering, preferred molar ratios, and recycling. See, e.g., cols. 1-3.

*2. Ascertaining the differences between the prior art and the claims at issue –*

Wilen does not disclose the molar ratio between the acid and base in particular. March does not disclose the resolution of racemic mandelic acid with a resolving agent. The other references (i.e., the five US patents) do not use a cyclic amide as a resolving agent.

3. *Resolving the level of ordinary skill in the pertinent art* – the level of ordinary skill in the art may be found by inquiring into: (1) the type of problems encountered in the art; (2) prior art solutions to those problems; (3) the rapidity with which innovations are made; (4) the sophistication of the technology; and (5) the education level of active workers in the field. *Custom Accessories, Inc. v. Jeffrey-Allan Industries, Inc.*, 807 F.2d 855, 962 (Fed. Cir. 1986). All of those factors may not be present in every case, and one or more of them may predominate. *Envtl. Designs, Ltd. v. Union Oil Co.*, 713 F.2d 693, 696 (Fed. Cir. 1983).

Based on the typical education level of active workers in the field of organic chemistry, as well as the high degree of sophistication required to solve problems encountered in the art, the Examiner finds that a person of ordinary skill in the art would have at least a college degree in the field of organic chemistry and at least four years of work experience, i.e. a masters or doctorate level scientist.

4. *Considering objective evidence present in the application indicating obviousness or nonobviousness* – none.

*Conclusion* – the Federal Circuit stated "[o]bviousness does not require absolute predictability of success . . . all that is required is a reasonable expectation of success." *O'Farrell* at 903-904. *In the instant case*, the prior art cited above, taken as a whole, supports the conclusion that a person of ordinary skill in the art, at the time of invention, would have been motivated to try known options within their technical grasp in the art. Those options include the use of various resolving agents (*see, e.g.*, the references



provided as well as the full disclosure of Wilen, which provides tables of different resolving agents).

The Examiner finds that the substitution of one option for another (i.e., resolving agent) is within the technical grasp in the art and one of ordinary skill in the art would be willing to attempt as many options as needed until a preferred result is found. In this case, Claim 1 is generic, whereas Claims 2 & 3 are drawn to a particular subgenus of mandelic acids and cyclic amides. The Examiner suggests that the instant claims be limited to the scope of such claims in order to overcome this rejection.

#### ***Claim Objections***

Claims 2 & 3 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

#### ***Allowable Subject Matter***

Claims 9-16 are drawn to a subgenus of compounds according to formulae IIb, VI, Ia, and Ib. Said compounds are free of the prior art. The closest prior art are the salts disclosed in Wilen. *See, e.g.*, p. 73 (having a *meta*-methoxy but no *meta*-chloro functionality).

***Telephone Inquiry***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jason M. Nolan whose telephone number is (571) 272-4356 and e-mail is [Jason.Nolan@uspto.gov](mailto:Jason.Nolan@uspto.gov). The examiner can normally be reached Monday - Friday (9:00AM - 5:30PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M<sup>c</sup>Kane, may be contacted at [Joseph.McKane@uspto.gov](mailto:Joseph.McKane@uspto.gov) or (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system, (Private PAIR or Public PAIR). Status information for unpublished applications is available through Private PAIR only. For information about the PAIR system, see <http://pair-direct.uspto.gov>. For questions on Private PAIR system, contact the Electronic Business Center at (866) 217-9197.

/Jason M. Nolan/

Examiner, Art Unit 1626